UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,495	04/24/2006	Nicolas Mermod	3024-119	1575

46002 7590 07/19/2010

JOYCE VON NATZMER
PEQUIGNOT + MYERS LLC
200 Madison Avenue
Suite 1901
New York, NY 10016

EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
07/19/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/595,495	MERMOD ET AL.	
	Examiner	Art Unit	
	CELINE X. QIAN	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-17,23,24,26,28,34,42-45,48,49,51,55,62-72,74-103 and 105-121* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65-68,70,71,74-79,81,83-89,91,101,102,106-108 and 111-121* is/are rejected.

7)☒ Claim(s) *106,107 and 121* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 15-17,23,24,26,28,34,42-45,48,49,51,55,62-64,69,72,80,82,90,92-100,103,105,109 and 110.

DETAILED ACTION

Claims 15-17, 23, 24, 26, 28, 34, 42-45, 48, 49, 51, 55, 62-72, 74-103, 105-121 are pending in the application. Claims 15-17, 23, 24, 26, 28, 34, 42-45, 48, 49, 51, 55, 62-64, 69, 72, 80, 82, 90, 92-100, 103, 105, 109 and 110 are presented as withdrawn claims. Claims 65-68, 70, 71, 74-79, 81, 83-89, 91, 101, 102, 106-108, 111-121 are currently under examination.

Election/Restrictions

The restriction requirement has been made final in the previous office action mailed on 10/28/09 (detailed reason on pages 2-3). In response, Applicants assert that SEQ ID NO: 24-27 are not only united by their source, i.e. they are all novel human MAR elements, they also share the common structure of being rich in AT and TA dinucleotides, which links to their common protein increasing activity greater than that of cLyMAR. Applicants argue that the claims are amended to include that activity of increasing protein production to levels greater than cLysMAR, a limitation not disclosed by Kries et al. Applicants thus conclude that claims 72, 80, 82, 90, 103 and 105 share structural features linked to a shared inventive and novel activity, and requested these claims be rejoined.

The above statement has been fully considered. In response to the arguments directed to the common structure between SEQ ID NO: 24-27, Applicants' attention is directed to the guideline set forth in MPEP 1850:

> Where a single claim defines alternatives of a Markush group, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, is considered met when the alternatives are of a similar nature. When the Markush grouping is for alternatives of chemical compounds, the alternatives are regarded as being of a similar nature where the following criteria are fulfilled:
> (A) all alternatives have a common property or activity; AND
> (B) (1) a common structure is present, that is, a significant structural element is shared by all of the alternatives; OR
> (B) (2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the

> invention pertains.
> The phrase "significant structural element is shared by all of the alternatives" refers to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity.
> The phrase "recognized class of chemical compounds" means that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention, i.e. each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

The claimed DNA sequences of SEQ ID NO: 24-27 have a common property being increasing protein production activity greater than that of chicken lysozyme MAR, which satisfy part (A). However, B1 requires that a common structure, a significant structural element is shared by all of the alternatives. The sequences of SEQ ID NO: 24-27 does not share a significant structural elements based on the nucleic acid sequences because 1) they do not have significant sequence similarity; 2) the common structure of 10% TA and or 12% AT on a stretch of 100 contiguous base pair, and comprise a binding site for DNA binding protein, as alleged by Applicants that it is essential to the common property, does not make a contribution over prior art, as evidenced by Michalowski et al. (see for example SEQ ID NO: 5, the first 100 nucleotides, which comprises more than 10 TA dinucleotide). With regard to the requirement of B2, unless Applicants declare that each sequence of SEQ ID NO: 24-27 could be substituted one for the for the intended results, the prior art does not recognize that structure of 10% TA and or 12% AT on a stretch of 100 contiguous base pair, and comprise a binding site for DNA binding protein will behave in the same way for increasing protein production activity greater than that of chicken lysozyme MAR. Therefore, the restriction requirement is proper. With regard to

claims 72, 80, 82, 90, 103 and 105, Applicants are reminded that these claims have been examined in the previous office action to the extend it read on SEQ ID NO: 25.

Specification

Acknowledgement is made of the submission of amended specification for deleting hyperlinks. The objection to this part has been withdrawn. However, the specification remains being objected to for following reason.

The use of the trademark such as SMART scan, SMARTest, etc. has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

In response, Applicants assert that the specification maintains the proprietary nature of the SMAR Scan^{R} by using R trademark registration symbol and by capitalizing "SMAR," and described generically in paragraph 84.

This argument has been considered but deemed unpersuasive. MPEP 608.01 (v) set forth "Trademarks should be identified by capitalizing each letter of the mark (in the case of word or letter marks) or otherwise indicating the description of the mark (in the case of marks in the form of a symbol or device or other nontextual form)." This requirement cannot be overlooked.

Claim Objections

In response to the objection to claims that contain non-elected subject matter, Applicants canceled 73 and 104, and withdrawn the rest from consideration. The objection is thus moot.

Claims 106, 107 and 121 are objected to because they depend on non-elected claim 105, thus contain non-elected subject matter. This is resulted from the amendment.

Applicant is advised that should claim 106 be found allowable, claim 121 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65-91, 101-104, 108, 112-121 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555,

1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

In analyzing whether the written description requirement is met, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. Claim 65 recites "a purified and isolated DNA sequence that comprises at least one bent DNA element comprising at least 10% of the TA and/or 12% AT on a stretch of 100 base pairs, and at least one binding site for a DNA binding protein, which has protein production increasing activity greater than that of cLysMAR." The claimed invention encompasses a large genus of nucleic acid sequences of varying length (longer or equal to 100 base pair) which have at least 10% of the TA and/or 12% AT on a stretch of 100 base pairs, regardless whether they possess protein production increasing activity greater than that of cLysMAR in any setting (*in vitro, in vivo*, or in transgenic organism). The specification discloses identification of MAR sequences which may increase protein expression in CHO cells through bioinformatics computational algorithms. The specification discloses 4 sequences (1-68, 1-6, 1-42 and X-S29) picked out from such potential MARs which displays protein production increasing activity greater than that of the 5' chicken lysozyme MAR when linked to the expression construct in CHO cells. The specification discloses all these sequences have a high AT/TA value (mean about 35%, see Table 6) and comprises potential transcription factor binding

sites. However, the specification does not disclose whether any sequence with 10% TA and/or 12% AT on a stretch of 100 base pairs and a DNA binding site would have protein producing increasing activity in any setting (*in vitro, in vivo* or in transgenic organism).

The information within the prior art at the time of filing does not make up for the deficiency in the specification for describing the structural element that is linked to the claimed function. The specification indeed states in the background section "no clear cut MAR consensus sequence has been found...(page 2, line 37)" and "the identification of MAR by biochemical studies is a long and unpredictable process, various results can be obtained depending on the assay (see page 2, lines 46-47)." With regard to predicting MAR sequence by *in silico* method, the specification teaches all available tools are limited by factors such as poor specificity, the lack of confirmation of large amount of hypothetical MARs identified by such tool, and thus, many of such tools becomes useless to identify potent genetic elements with regard to efficient increasing recombinant protein production (see page 3, 1st-3rd paragraph). Girod et al., published in 2007 (see IDS), 4 years after the date of filing of the present application, state "only a few MARs have been conclusively identified from an estimated number of 50,000 or more per genome." Girod et al. further teach that "although the nuclear matrix binding function of MARs is conserved from plants to mammals, their DNA sequence is highly polymorphic, and their activities could not be ascribed to any simple DNA motif. Thus, MAR function has often been related to structural properties rather than to its primary sequence, such as the high DNA strand unwinding and unpairing susceptibility of A+T rich sequences and a high potential for denaturation of the double helix. Whether these features contribute to the transcriptional activity of MARs is yet unknown." Girod et al. then teaches a method of

identifying MAR sequences based on the prediction of active MAR sequences have a high potential to accommodate curvature, a deep DNA major groove and a wide minor groove, a weak correlation with DNA melting temperature and the presence of certain transcription factors such as SATB1, NMP4 and homeobox proteins (see page 748, 2nd col., and page 749). Girod et al. disclose that 1,566 sequences from the human genome were identified using above parameter at stringent condition (see page 749, bridging paragraph). Girod et al. disclose that none of the 1,566 sequence can be completely aligned on the mouse genome, and suggesting different primary sequence may contribute to species specificities. Girod et al. further selected several putative MAR sequences based on the basis of their high computed score, location near known ubiquitously expressed genes (to avoid tissue specific activity), and have core elements of various length and/or enriched in various combination of potential transcription factor binding sites (see page 749, last paragraph of col.2). Girod et al. disclose that 6 out 7 such sequences increased expression of a reporter in stably transfected polyclonal CHO cells substantially. Girod et al. disclose that one of the non-activator, 1-15, does not exhibit obvious difference between active and inactive sequences, wherein it also has highly enriched AT and TA dinucleotides (70%), and no qualitative or quantitative difference between core sequences of functional and inactive sequences. Girod et al. assert that the mere presence of an (A+T) rich core elements does not suffice to activate gene expression, and the lack of activity may result from the lack of tissue specific activities in CHO and/or from the requirement of additional DNA features (page 750, 2nd col., 2nd paragraph). Girod et al. suggest that gene activation by MARs may rely on the positioning of a nucleosome in the vicinity of transcription factor binding sites, whereas DNA curvature motif alone is not sufficient for transcriptional activity (see page 752, 1st

col., 1st paragraph). Girod et al. acknowledges that MARs display a bewildering array of activities that have been difficult to ascribe to any specific DNA motif (see page 751, 2nd col., 1st sentence of last paragraph).

In view of the teaching in the prior art, it appears that there is no consensus agreement that any of the specific DNA motif may be ascribe to various activities of MARs, especially the protein expression enhancing activity. As such, whether a DNA sequence comprising one bent element comprising at least 10% of the dinucleotide TA an/or at least 12% of the dinucleotide AT on a stretch of 100 contiguous base pairs; and at least one binding site for a DNA binding protein can increase protein production is unpredictable. The specification discloses only 4 (4 out of more than one thousand that selected by the computer program) nucleic acids that have the recited structural and can increase protein production in CHO cells greater than that of cLysMAR, it thus fails to describe a representative of species of nucleic acids having the structural properties comprising at least 10% of the dinucleotide TA an/or at least 12% of the dinucleotide AT on a stretch of 100 contiguous base pairs; and at least one binding site for a DNA binding protein that can have the functional property of increasing protein production in any system than that of cLysMAR. Moreover, the specification fails to describe other identifying characteristic of the claimed genus of nucleic acids that has the recited structure and function. In other words, the specification fails to describe a nexus between the claimed structure and the function of increasing protein production in any system than that of cLysMAR. Nucleic acids that of various lengths (larger or equal than 100 base pair) comprise 10% of the dinucleotide TA an/or at least 12% of the dinucleotide AT on a stretch of 100 contiguous base pairs may have the property of being a curved DNA and/or bind matrix protein (DNA binding

protein is not limited to transcription factors, but applies to matrix binding protein as well), whether they have the function of increase protein expression *in vitro* (in cell free system) or *in vivo* or more than that of cLysMAR is unpredictable because the specification fails to establish such a nexus. Similarly, although the art recognizes that the MARs having transcription activity generally has a wider minor groove and deeper major groove and a low melting temperature, the exact value for such parameters possessed by a nucleic acid molecule that has protein increasing activity greater than that of cLysMAR is not precisely determined even years after the application is filed. The application also fails to describe such parameter for the claimed genus of nucleic acids that alleged have protein production increasing activity greater than that of cLysMAR. Since the specifications fails to establish a structural and functional relationship, and the prior art does not make up such deficiency, the skilled artisan would not be able to envision the common structure of the claimed nucleic acid required for its function. Therefore, the claimed DNA is not sufficiently described by the instant specification. With regard to variants or fragments of SEQ ID NO: 25, it is not sufficiently described because the specification does not describe which fragment, and or what type of variant of this DNA molecule have the protein producing increasing activity. Lastly, since the claimed DNA is not sufficiently described, the vector and host cell comprise said DNA also lack description for same reason as set above. Thus, the specification fails to describe the invention in such a way to convey a skilled artisan that the inventors had possession of the invention at the time the application was filed.

Response to Arguments

In response to this rejection, Applicants argue that Girod's method does not take advantage of the tool, including selection tool, provided and disclosed by the present specification to distinguish between functional and sequences that indeed increase protein production activity greater than that of chicken lysozyme MAR. Applicants assert that the specification provides a bio-informatic tool to retrieve relevant sequences, and provides an example (6) details the identification of super MARs having AT dinucleotide frequencies greater than 12% and TA frequencies greater than 10% out of a total of 100 base pair DNA, with the most efficient MARs displaying mean values around 35% of the two nucleotide pairs. Applicants assert that 1757 potential super MARs are further selected using different criteria, including checking for transcription factor binding sites. Applicants further assert that examples 11 and 16 have shown that taken together the tools provided by the specification are able to identify some "super" MARs that increase the expression of a recombinant protein very significantly above the expression drive by the chicken lysozyme MAR. Applicants also states claims 112-115 fall outside the rejection because the office action does not make specific rejections to claims 112-115 and only focuses on the recitation in claim 65.

The above arguments have been fully considered but deemed unpersuasive. The detailed reason for lack of description of the claimed invention was set forth in the previous office action and above. In response to the argument directed to specific tool described in the specification, Applicants are reminded that the claimed invention is not drawn to such a tool, rather, it is drawn to purified and isolated DNA sequences having recited structure and function. The rejection set

forth above has determined that the invention is in emerging and unpredictable technologies.

MPEP 2163.02 set forth

> "for inventions in emerging and unpredictable technologies, or for inventions characterized by factors not reasonably predictable which are known to one of ordinary skill in the art, more evidence is required to show possession. For example, disclosure of only a method of making the invention and the function may not be sufficient to support a product claim other than a product-by-process claim. See, e.g., Fiers v. Revel, 984 F.2d at 1169, 25 USPQ2d at 1605; Amgen, 927 F.2d at 1206, 18 USPQ2d at 1021. Furthermore, disclosure of a partial structure without additional characterization of the product may not be sufficient to evidence possession of the claimed invention. See, e.g., Amgen, 927 F.2d at 1206, 18 USPQ2d at 1021 ("A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated.") (citations omitted). In such instances the alleged conception fails not merely because the field is unpredictable or because of the general uncertainty surrounding experimental sciences, but because the conception is incomplete due to factual uncertainty that undermines the specificity of the inventor's idea of the invention. Burroughs Wellcome Co. v. Barr Laboratories Inc., 40 F.3d 1223, 1229, 32 USPQ2d 1915, 1920 (Fed. Cir. 1994). Reduction to practice in effect provides the only evidence to corroborate conception (and therefore possession) of the invention. Id."
> ...
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004)"

In the instant case, the claimed MARs encompasses a large genus of nucleic acid sequences of natural or synthetic nature that varying length (longer or equal to 100 base pair)

which have at least 10% of the TA and/or 12% AT on a stretch of 100 base pairs. However, the specification only disclosed 4 sequences (1-68, 1-6, 1-42 and X-S29) picked out from such potential MARs which displays protein production increasing activity greater than that of the 5' chicken lysozyme MAR when linked to the expression construct in CHO cells. The specification discloses all these sequences have a high AT/TA value (mean about 35%, see Table 6) and comprises potential transcription factor binding sites. Four examples out of potentially unlimited number of MARS that possess the claimed activity cannot be considered to be a representative number of species because of the unpredictable nature of MARs as discussed above. The specification also fails to describe the structural requirement that will contribute the super MAR activity. Although claim 65 recites the structural requirement being "have at least 10% of the TA and/or 12% AT on a stretch of 100 base pairs, and have transcription binding site," the chicken lysozyme MAR in fact satisfy this structural requirement (12.03% AT and 10.29% TA, see page 31, table 6). The skilled artisan would thus question whether this structural requirement is linked to its function of having protein producing activity greater than chicken lysozyme MAR because it cannot have more activity than itself. Lastly, although claims 112-115 were not addressed specifically in the rejection above, they also fall within the rejection for same rationale as discussed in the previous office action and above. Although claim 112 recites a higher percentage of AT/TA dinucleotide, 33%, the specification only describe one example, P1-68, has increased protein production activity higher that of chicken lysozyme MAR. The unpredictability is evidenced by Girod's disclosure that a sequence having more than 70% dinucleotide content fails to activate transcription. Therefore, the specification fails to provide adequate description to the claimed genus of MARs, and this rejection is maintained.

Newly added claims 116-121 reciting sequence of SEQ ID NO: 25 are also included in this rejection because the claims also encompass "complementary, fragment and variant." Since the structural and functional relationship is not established, the skilled artisan cannot envision the structure of said "complementary, fragment and variant" based on the recited activity.

The rejection of claims under 35 U.S.C 112 2nd paragraph has been withdrawn in light of the amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 106 and 121 are rejected under 35 U.S.C. 102(b) as being anticipated by Klehr et al. (see IDS)

Klehr disclose synthetic MAR comprising human β-interferon Domain MAR comprising linker such as EcorRI and BamHI (see page 1265, 2nd col., 1st paragraph, and Figure 1). Since the specification does not describe what constitutes a variant of SEQ ID NO: 25, the disclosed MAR from Klehr et al. is considered to meet this limitation. Therefore, Klehr disclose the instantly claimed invention.

Response to Arguments

In response to this rejection, Applicants argue that variants are described as "nucleotide sequences that vary from the reference sequence by conservative nucleotide substitution, whereby one or more nucleotides are substituted by another with the same characteristics. Applicants thus argue that the prior art sequence does not anticipate this claim.

The above argument has been fully considered but deemed unpersuasive. While nucleotide conservative substitution in the context of coding sequence is clearly defined in art, such definition does not apply to MAR sequence because they do not encode a protein product. In other word, it is unclear what type of replacement constitutes "substituted by another with the same characteristics." (i.e. A->T, A->C?) The specification does not teach what type of replacement or how much nucleotide of replacement will still have the claimed property. Moreover, the statement of "one or more nucleotides" provides a non-limiting number of substitution/replacement of the nucleotides of SEQ ID NO: 25. It can potentially result in a nucleotide sequence that has no sequence homology with SEQ ID NO: 25. Therefore, the synthetic MAR comprising human β-interferon Domain MAR comprising linker such as EcorRI and BamHI meet this limitation.

Claims 112-115 are rejected under 35 U.S.C. 102(b) as being anticipated by Michalowski et al (US 6,245,974). This rejection has been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 107 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klehr et al.

The teaching of Klehr et al. was discussed above. However, Klehr et al. do not teach a MAR with BglII-BamHI linker.

It would have been obvious to an ordinary skill in the art to add a BglII-BamHI linker to a synthetic MAR sequence based on the choice of appropriate multiple cloning sites on the vector. Klehr et al. already demonstrated the use of BamHI and EcorRI sites to clone the MAR into a vector. The ordinary skill in the art would pick appropriate restriction sites to clone DNA sequence into a vector, wherein such knowledge and reagent is readily be available to an ordinary artisan at the time of filing, for example, the New England biolab catalog. Adding different linkers including BamHI and BglII would have been routine experimentation to an ordinary artisan at the time the invention was made. Therefore, the claimed invention would have been *prima facie* obvious in view of the cited reference.

Applicants presented same arguments as directed to claim 106 as set forth above. This is not considered persuasive for reason given above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CELINE X. QIAN whose telephone number is (571)272-0777. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Celine X Qian /
Primary Examiner, Art Unit 1636